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EXAMINER	
GABEL, GAILENE	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 09/01/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/492,214	STEMMLER ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-7,9-16,19,21,23,33-36 and 42-59* is/are pending in the application.

4a) Of the above claim(s) *46 and 48-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-7,9-16,19,21,23,33-36,42-45 and 47* is/are rejected.

7)☒ Claim(s) *19 and 21* is/are objected to.

8)☒ Claim(s) *2-7,9-16,19,21,23,33-36 and 42-59* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/17/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. Applicant's amendment and response filed 6/17/04 is acknowledged and has been entered. Claims 42 and 47 have been amended. Claims 48-59 have been added. Claim 46 remains withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being claim drawn to a non-elected invention.

2. Newly submitted claims 48-59 are directed to inventions that are independent or distinct from the invention originally claimed for the following reasons:

Claims 48-59 are drawn to methods for qualitative or quatitative determination of analyte wherein the solid phase coated with a quenching substance also includes thereto a binding partner which takes part in binding interaction between components of an assay.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 46 and 48-59 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Accordingly, claims 2-7, 9-16, 19, 21, 23, 33-36, and 42-59 are pending. Claims 2-7, 9-16, 19, 21, 23, 33-36, 42-45, and 47 are under examination.

Rejections Withdrawn

3. In light of Applicant's argument, the rejection of claims 2-4, 9-11, 35, 42, 44, 45, 47 under 35 U.S.C. 102(e) as being anticipated by Selvin (US Patent 6,667,179) is hereby, withdrawn.

4. In light of Applicant's amendment and argument, the rejection of claims 2-4, 6, 7, 9-13, 35, 42-45, 47 under 35 U.S.C. 102(e) as being anticipated by Mirkin et al. (US Patent 6,361,944) is hereby, withdrawn.

5. In light of Applicant's amendment and argument, the rejection of claims 5, 14-16, 21, 23, 33, 34, and 36 under 35 U.S.C. 103(a) as being unpatentable over Mirkin et al. (US Patent 6,361,944) in view of Hargreaves (US 6,121,055) is hereby, withdrawn.

6. In light of Applicant's amendment and argument, the rejection of claim 19 under 35 U.S.C. 103(a) as being unpatentable over Mirkin et al. (US Patent 6,361,944) in view of Hargreaves (US 6,121,055), and in further view of Dixon et al. (US 5,381,224) is hereby, withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 2-7, 9-16, 19, 21, 23, 33-36, 42-45, and 47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 5 remains ambiguous in reciting, "the analyte determination occurs" because it is unclear how a step of determination *occurs.* Perhaps, Applicant intends "determination is performed or effected".

Claim 42 is vague and indefinite because it remains unclear what functional cooperative relationship exists between the quenching substance and each of 1) the labeled reagent bound to the analyte, and the 2) unbound labeled reagent, in order to thus, cause at least some of the signal from unbound labeled reagent to be suppressed. The claim only recites that [the step of] incubating of the sample containing the analyte with labeled reagent and a solid phase coated with a quenching substance allows at least some of the labeled reagent to bind the analyte; hence, it is unclear what functional relationship exists between the quenching substance and each of the analyte, the labeled reagent that binds, and the labeled reagent that does not bind (unbound). Please clarify.

Claim 47 is vague and indefinite because it remains unclear what functional cooperative relationship exists between the quenching substance and each of 1) labeled analyte bound to the reagent, and the 2) unbound labeled analyte, in order to thus, cause at least some of the signal from unbound labeled analyte to be suppressed. The claim only recites that [the step of] incubating of the sample containing the labeled analyte with a reagent and a solid phase coated with a quenching substance allows at least some of the labeled analyte to bind the reagent; hence, it is unclear what functional relationship exists between the quenching substance and each of the

reagent, labeled analyte that binds, and the labeled analyte that does not bind (unbound). Please clarify.

Accordingly, claims 42 and 47 remain rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 2-7, 9-16, 23, 33-36, 42-45, and 47 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for qualitative and quantitative determination of analyte comprising: incubating a sample containing analyte with a labeled reagent and a solid phase coated with a quenching substance to allow labeled reagent to bind to the analyte, exciting the sample so as to generate signal from the bound labeled reagent, and 1) measuring the signal generated only from one phase of the signal generating phases containing the bound-labeled reagent by spatially staggered measurement, or 2) measuring the signal generated only from a defined volume element of the liquid phase of the signal generating phases containing the bound-labeled reagent, thereby quantitatively or qualitatively determining the

analyte without physically separating unbound and bound labeled reagent; does not reasonably provide enablement for measuring any and all of the signal generating phases, i.e. liquid phase and solid phase, containing the bound labeled reagent which is encompassed by the claimed invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

As set forth in In re Wands, 858 F .2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988), enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Factors to be considered in determining, whether a disclosure would require undue experimentation include 1) the nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the quantity of experimentation necessary, 7) the relative skill of those in the art, and 8) the breadth of the claims.

The nature of the invention- the invention is directed to a method for quantitative or qualitative determination of an analyte wherein a sample containing analyte, a labeled reagent, and a solid phase coated with a quenching substance are incubated to allow the labeled reagent to bind to the analyte, and excited so as to generate signal from the bound labeled reagent, and further measured to thereby quantitatively or qualitatively determine the analyte concentration without physically separating unbound and bound labeled reagent. Measurement signal from only one of the signal generating phases present which contain bound labeled reagent is obtained by space-staggered

measurement, and each individual measurement signal represents the intensity of fluorescence occurring at each position. Alternatively, a single measurement signal corresponding to a defined volume segment of the liquid phase, preferably having a diameter of 40 um or less, can also be obtained by illuminating the sample volume segment with a laser and only the generated signal of this volume segment is measured.

The state of the prior art- the prior art of record fails to disclose a method as claimed wherein the bound and unbound labeled reagent contained in the mixture are not physically separated when obtaining measurement of bound labeled reagent, to provide a quantitative or qualitative determination of the analyte.

The predictability or lack thereof in the art- there is no predictability based on the instant specification that the claimed method will work to provide accurate quantitative or qualitative measure of analyte concentration.

The amount of direction or guidance present- appropriate guidance is provided by the specification for the claimed method to work if the signal generated only from a phase of the signal generating phases (liquid and solid) containing the bound-labeled reagent is measured by spatially staggered measurement; or the signal generated only from a defined volume element of the liquid phase of the signal generating phases containing the bound-labeled reagent is measured, in quantitatively or qualitatively determining the analyte without physically separating unbound and bound labeled reagent. However, the specification fails to provide any guidance to enable the claimed

method to function, without physically separating unbound and bound labeled reagent, by merely measuring the signal generated from the bound labeled reagent, as claimed.

The presence or absence of working examples- working examples are provided in the specification that show a method for quantitative or qualitative determination of an analyte wherein a sample containing analyte, a labeled reagent, and a solid phase coated with a quenching substance are incubated to allow the labeled reagent to bind to the analyte, then excited so as to generate signal from the bound labeled reagent, and wherein the signal generated only from a phase of the signal generating phases containing the bound-labeled reagent is measured by spatially staggered measurement, or the signal generated only from a defined volume element of the liquid phase of the signal generating phases containing the bound-labeled reagent is measured, without physically separating unbound and bound labeled reagent. There are no working examples that show analogous results by merely measuring the signal generated from the bound labeled reagent, as claimed.

The quantity of experimentation necessary- it would require undue amount of experimentation for the skilled artisan to make and use the method as claimed.

The relative skill of those in the art-the level of skill in the art is high.

The breadth of the claims- as recited, the instant claims are directed to a method for quantitative or qualitative determination of an analyte wherein a sample containing analyte, a labeled reagent, and a solid phase coated with a quenching substance are incubated to allow the labeled reagent to bind to the analyte, excited so as to generate signal from the bound labeled reagent, and measured, to thereby quantitatively or

qualitatively determine the analyte concentration without physically separating unbound and bound labeled reagent; and without any regard as to how interference by unbound components is removed to thus, obtain accurate detection and quantitation of analyte.

In pages 9 and 10 of the disclosure, Applicant provides that in performing the claimed invention for measuring the bound labeled reagent without physically separating unbound and bound labeled reagent, a qualitative and quantitative determination of analyte concentration can be obtained when measurement signal from only one of the signal generating phases present which contain bound labeled reagent is obtained by space-staggered measurement, and each individual measurement signal represents the intensity of fluorescence occurring at each position. Alternatively, a single measurement signal corresponding to a defined volume segment of the liquid phase, preferably having a diameter of 40 um or less, can also be obtained by illuminating the sample volume segment with a laser and only the generated signal of this volume segment is measured. While the specification exemplifies methods of qualitatively and quantitatively determining analyte by a series of space-staggered measurement of a signal generating phase or a single measurement of a signal of a defined volume segment of the liquid phase, of a mixture containing bound and unbound components, the specification does not show any working examples of the claimed method. The specification does not provide any teaching that suggests that a quantitative or qualitative determination of an analyte in a sample mixture containing analyte, a labeled reagent, and a solid phase coated with a quenching substance wherein the labeled reagent is allowed to bind to the analyte, and excited so as to

generate signal from the bound labeled reagent, and can be measured as claimed, without physically separating unbound and bound labeled reagent. While it is not necessary to show working examples for every possible embodiment, there should be sufficient teachings in the specification that would suggest to the skilled artisan that the breadth of the claimed method is enabled. This is not the case in the instant specification.

In view of the teachings of In re Wands, 8 USPQ2d 1400, it has been determined that the level of experimentation required to enable the breadth of the claims is undue. It has been set forth above that 1) the experimentation required to enable the claimed method for determining a qualitative or quantitative determination of analyte, would be great as 2) there is no experimental evidence provided that would indicate that the claimed method of measuring analyte would actually work without physically separating unbound and bound labeled reagent; 3) there is no proper guidance that shows that the claimed method of measuring analyte would work without physically separating unbound and bound labeled reagent in the instant specification, 4) the nature of the invention is a method for quantitative or qualitative determination of an analyte wherein a sample containing analyte, a labeled reagent, and a solid phase coated with a quenching substance are incubated to allow the labeled reagent to bind to the analyte, excited so as to generate signal from the bound labeled reagent, and then measured to thereby quantitatively or qualitatively determining the analyte without physically separating unbound and bound labeled reagent; measurement signal from only one of the signal generating phases present which contain bound labeled reagent is obtained

by space-staggered measurement, and each individual measurement signal represents the intensity of fluorescence occurring at each position or alternatively, a single measurement signal corresponding to a defined volume segment of the liquid phase, preferably having a diameter of 40 um or less, can also be obtained by illuminating the sample volume segment with a laser and only the generated signal of this volume segment is measured, 5) the relative skill of those in the art is high, yet 6) the state of the prior art has been shown to be unpredictable as evidenced by the fact that no prior art has been cited that disclose a method as claimed wherein the bound and unbound labeled reagent contained in the mixture are not physically separated and measured to provide a quantitative or qualitative determination of the analyte, and lastly 7) the claims broadly recite a method directed to quantitative or qualitative determination of an analyte wherein a sample containing analyte, a labeled reagent, and a solid phase coated with a quenching substance are incubated to allow the labeled reagent to bind to the analyte, excited so as to generate signal from the bound labeled reagent, and measured, to thereby quantitatively or qualitatively determine the analyte concentration, without physically separating unbound and bound labeled reagent; without specifically stating how this can be done without undue experimentation.

Therefore, it is maintained that one of ordinary skill in the art could not make and use the invention as claimed without undue experimentation.

Response to Arguments

9. Applicant's arguments filed 6/17/04 have been fully considered but they are not persuasive.

A) In response to the rejection under 35 USC 112, second paragraph, indefinite of claims 42 and 47, Applicant submits that in at least one embodiment, binding between the labeled reagent and the analyte causes the quenching substance to quench or suppress at least some of the signal originating from the unbound labeled reagent.

In response, while the binding between the labeled reagent and the analyte causes the quenching substance to quench or suppress at least some of the signal originating from the unbound labeled reagent, it remains unclear what structural and functional cooperative relationship exists between the quenching substance and each of the labeled reagent bound to the analyte, and the unbound labeled reagent, in order to thus, cause at least some of the signal from unbound labeled reagent to be suppressed. See discussion supra. Does Applicant intend for the quenching substance to bind the labeled reagent bound to the analyte, or bind the unbound labeled reagent, etc.; hence, causing suppression of at least some signal from unbound labeled reagent.

Allowable Subject Matter

10. Claims 19 and 21 are objected to for depending from rejected claims. Claims 19 and 21 would be allowable if rewritten to overcome the rejections under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (571) 272-0820. The examiner can normally be reached on Monday, Tuesday, and Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gailene R. Gabel
Patent Examiner
Art Unit 1641
August 24, 2004

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641
8/30/04